Integrative genomic and functional analyses reveal neuronal subtype differentiation bias in human embryonic stem cell lines.

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Public Summary:
The self-renewal and differentiation potential of human embryonic stem cells (hESCs) suggests that hESCs could be used for regenerative medicine, especially for restoring neuronal functions in brain diseases. However, the functional properties of neurons derived from hESC are largely unknown. Moreover, because hESCs were derived under diverse conditions, the possibility arises that neurons derived from different hESC lines exhibit distinct properties, but this possibility remains unexplored. To address these issues, we developed a protocol that allows stepwise generation from hESCs of cultures composed of approximately 70-80% human neurons that exhibit spontaneous synaptic network activity. Comparison of neurons derived from the well characterized HSF1 and HSF6 hESC lines revealed that HSF1- but not HSF6-derived neurons exhibit forebrain properties. Accordingly, HSF1-derived neurons initially form primarily GABAergic synaptic networks, whereas HSF6-derived neurons initially form glutamatergic networks. microRNA profiling revealed significant expression differences between the two hESC lines, suggesting that microRNAs may influence their distinct differentiation properties. These observations indicate that although both HSF1 and HSF6 hESCs differentiate into functional neurons, the two hESC lines exhibit distinct differentiation potentials, suggesting that they are preprogrammed. Information on hESC line-specific differentiation biases is crucial for neural stem cell therapy and establishment of novel disease models using hESCs.

Scientific Abstract:
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